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Acute glucocorticoid effects on response inhibition in borderline personality disorder

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Summary
Introduction: Growing evidence suggests inhibition dysfunctions in borderline personality disorder (BPD). Moreover, abnormalities in hypothalamic-pituitary-adrenal (HPA) axis functioning have also been found in BPD patients. In healthy individuals, response inhibition has been sensitive to acute stress, and previous research indicates that effects mediated by the HPA axis become particularly apparent when emotional stimuli are processed. This study aimed to explore the influence of acute hydrocortisone administration on response inhibition of emotional stimuli in BPD patients compared to healthy control participants.
Methods: After a single administration of 10 mg hydrocortisone or placebo, 32 female BPD patients and 32 healthy female participants performed an adapted emotional go/no-go paradigm to assess response inhibition for emotional face stimuli in a cross-over study.
Results: Acute cortisol elevations decreased the reaction times to target stimuli in both BPD patients and healthy controls. Patients and controls did not differ in task performance; however, BPD patients with comorbid posttraumatic stress disorder (PTSD) displayed longer reaction times than patients without PTSD. In contrast, the occurrence of comorbid eating disorder had no

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significant impact on go/no-go performance. No significant interaction effect between the treatment condition and the emotional valence of the face stimuli was found.
Conclusions: Acute hydrocortisone administration enhances response inhibition of face stimuli in BPD patients and healthy controls, regardless of their emotional valence. Our results agree with the suggestion that moderate cortisol enhancement increases the inhibition of task-irrelevant distracters.

1. Introduction

Borderline personality disorder (BPD) is a complex and serious mental disorder characterized by a pervasive pattern of instability in the regulation of emotion, interpersonal relationships, self-image, and impulse control (Skodol et al., 2002), indicating a diminished inhibitory control over behavior, emotion, and cognition (Fertuck and Stanley, 2006). Accordingly, impaired inhibitory processes have been assumed to be core features in BPD (Domes et al., 2006) and might also involve deficits in response inhibition. Response inhibition refers to the ability to suppress a cognitive expectation and/or motoric behavior in order to follow a different behavioral directive, expectation, or cognitive rule (Fertuck and Stanley, 2006). The go/no-go task is a classic paradigm that has been applied to BPD patients to investigate response inhibition. The paradigm has indicated deficits in response inhibition related to BPD, resulting in abnormally fast reaction times and a higher frequency of commission errors in BPD patients compared to healthy participants (Dinn et al., 2004; Rentrop et al., 2008). However, others failed to show impaired response inhibition in BPD (Kunert et al., 2003). Notably, inhibitory dysfunctions in BPD might become particularly apparent when such individuals process emotional stimuli (Domes et al., 2006; Krause-Utz et al., 2012; Mensebach et al., 2009; Silbersweig et al., 2007).

Given that exposure to early life stress is considered to be a major risk factor for developing BPD (Johnson et al., 1999; Zanarini et al., 1997), a growing number of studies have investigated stress-related abnormalities in BPD patients (Wingenfeld et al., 2010b; Zimmerman and Choi-Kain, 2009). Research on stress-related pathophysiology has particularly focused on the hypothalamic-pituitary-adrenal (HPA) axis, which constitutes the major neuroendocrine stress system (Heim and Nemeroff, 2002). Exposure to stress activates the HPA axis, which in turn regulates the release of glucocorticoids (GC) and is modulated by negative feedback. In a subset of studies, individuals with BPD showed enhanced cortisol levels under basal conditions, compared to healthy controls (Carvalho Fernando et al., 2012; Lieb et al., 2004; Wingenfeld et al., 2007). Overall, the findings of HPA activity in BPD were heterogeneous, with variability in results reflecting distinct patterns of comorbid psychopathology (Wingenfeld et al., 2010b).

Previous studies have repeatedly shown that GC hormones influence cognitive functions (Lupien et al., 2007), reflecting the high density of GC receptors located in several brain regions involved in memory and executive functions (Lupien and Lepage, 2001). In healthy individuals, most studies have focused on declarative memory tasks to demonstrate deficits in memory retrieval after GC treatment (Het et al., 2005). Similarly, cortisol administration has impaired working memory (Lupien et al., 1999; Wolf et al., 2001). A small and contradictory literature has evaluated the influence of GCs on response inhibition. In healthy men, Scholz et al. (2009) found go/no-go performance to be impaired after the induction of acute psychosocial stress, resulting in longer reaction times, compared to a resting condition. However, psychosocial stress induction has been associated with a stronger activation of the adrenergic system and cortisol-induced impairments in cognitive functions are supposed to require concurrent adrenergic activation (Elzinga and Roelofs, 2005). In contrast, Wolf et al. (2001) found no evidence for cortisol effects on response inhibition after a single administration of intravenous hydrocortisone when using a Stroop paradigm. More recently, research has begun to address the influence of stress on the processing of emotional stimuli during the inhibition of task-irrelevant information, i.e., tasks in which the emotional valence of the stimuli is not relevant for good task performance (Putman and Roelofs, 2011). In healthy young men, hydrocortisone (35 mg) enhanced performance in an adapted Sternberg task with emotional and neutral distracters, resulting in higher processing speed and fewer errors compared to a placebo group (Oei et al., 2009). Moreover, negative distracters interfered with task performance in the placebo group; in contrast, this interference effect was missing in the hydrocortisone group. The authors interpreted these results as evidence of a cortisol-mediated enhancement in the ability to suppress the interfering effects of emotional stimuli. In another study, using an emotional adaptation of the Stroop task, healthy men showed increased response times on trials for fearful compared to neutral face stimuli. This effect was abolished with the administration of 40 mg of hydrocortisone, resulting in comparable reaction times between both conditions (Putman et al., 2007). Collectively, empirical evidence suggests that acute cortisol elevation increases inhibition of task-irrelevant emotional (i.e., threat) stimuli in healthy individuals (Putman and Roelofs, 2011).

To our knowledge, the impact of acute hydrocortisone administration on inhibitory functions in BPD has not yet been examined. A single study produced by our group investigated cognitive functions, such as declarative and working memory, after cortisol administration in BPD (Wingenfeld et al., 2013). In this study, we found improving effects of cortisol on memory retrieval in BPD patients; in contrast, memory retrieval was impaired after cortisol administration in healthy controls. Similarly we found that, following hydrocortisone treatment, working memory improves in BPD when emotional distracters are included in the task but not when neutral distracters are presented. With regard to BPD accompanied by comorbid conditions, comorbid posttraumatic